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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/464,303	12/15/1999	GREGORY L. STAHL	B0801/7156	7348

7590 06/27/2003

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EXAMINER
VANDER VEGT, FRANCOIS P

ART UNIT	PAPER NUMBER
1644	20

DATE MAILED: 06/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application N .	Applicant(s)	
	09/464,303	STAHL ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34 and 36-41* is/are pending in the application.

4a) Of the above claim(s) *1-17 and 36-41* is/are withdrawn from consideration.

5)☒ Claim(s) *30-32* is/are allowed.

6)☒ Claim(s) *18-29,33 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on *22 April 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121. .

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The Examiner in charge of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to F. Pierre VanderVegt, Ph.D. in Art Unit 1644.

Claim 35 has been canceled previously.

Claims 1-34 and 36-41 are currently pending.

Claims 1-17 and 36-41 are withdrawn.

Claims 18-34 are the subject of examination in the present Office Action.

1. In view of applicant's amendment filed April 14, 2003, the following grounds of rejection are maintained for the reasons made of record.

Claim Rejections - 35 USC § 112

2. Claims 18-29 and 33-34 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Applicant's arguments filed April 9, 2003 have been fully considered but they are not persuasive. Applicant has amended claim 18 to recite that the "functional variants" of the claimed CDR3 regions are the result of "conservative substitutions," asserting that the specification at page 19, lines 23-31 provides adequate support for demonstrating that Applicant had possession of the claimed invention. The examiner respectfully disagrees with applicant's position. It is noted that the specification at page 19, line 23 through page 20, line 9 defines a "functional variant" of an MBL binding CDR3 region as a peptide having the sequence of one of the three monoclonal antibody CDR3 regions "with conservative substitutions therein." The same section defines seven groups of conservative substitutions included by the term. However, conservative substitutions are defined by the specification only in terms of an "amino acid substitution which does not alter the relative charge or size characteristics of the peptide in which the amino acid substitution is made" (page 19, lines 27-29, for example). Other than the assertion that conservative substitutions can be made to generate "functional equivalents," there is no evidence that the number of substitutions within a single CDR3 segment which can be tolerated without affecting the "fiunction" of the CDR3 has been even contemplated. While a single substitution may not "alter the relative charge or size characteristics of the peptide," substitution of 50 or 60% of the amino acids in a single CDR3 is likely to affect those properties. Further the specification does not define "functional

equivalents in terms of a particular function, only in terms of substitution. In other words, what amount of variation in what function can be tolerated for a variant peptide to be considered an "equivalent?" While it is well established in the specification that a function of the CDR3 regions of the clonal antibodies disclosed in the specification is to contribute to the binding of the antibody to MBL, there are no representative species of "functional variants" of the disclosed CDR3 regions which have been described that possess this, or any other, function of the disclosed CDR3 regions. Accordingly, the analogy to *Regents of the University of California v. Eli Lilly & Co.*, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997) remains applicable in the present situation. Accordingly, the ground of rejection is deemed proper.

3. Claims 18-29 and 33-34 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising an MBL inhibitor comprising an antibody produced by the hybridoma cell lines 2A9, 3F8 and hMBL1.2, does not reasonably provide enablement for the broader recitation of a composition comprising an MBL inhibitor comprising any peptide comprising an MBL CDR3 region of said antibodies, or any functional derivative thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Applicant traverses the rejection on the grounds that a working model is not needed, it would not require undue experimentation to show that a peptide consisting of one of the disclosed CDR3 peptides would bind to MBL, and applicant has shown that peptides such as the antibodies disclosed, F(ab) and $F(ab')_2$ fragments bind to MBL. Applicant's arguments are not persuasive. In the first case, while a peptide consisting of one of the disclosed CDR3 regions may very well bind to MBL, there is no adequate demonstation that longer peptides of, other than the CDR3 segment, undisclosed sequence will also bind to MBL. The amino acid residues which would flank the CDR3, while not directly involved with the act of binding will, nevertheless, affect the ability of that CDR3 to bind MBL, as each residue contributes to the overall 3D and charge characteristics of the peptide. Applicant argues, in regard to the Janeway reference (of record), that CDR1 and CDR2 "might further contribute partially to binding," in asserting that Janeway stresses the importance of CDR3 to binding. In fact, Janeway treats CDR1, CDR2, and CDR3 equally and does not emphasize any one over the others. Further, Janeway clearly shows that not only are all three CDRs important, but the intervening sequences contribute significantly to the 3-dimensional relationship of CDR1, CDR2, and CDR3 to one another, orienting the CDRs properly for forming the binding site. Applicant's further contention that peptides comprising the CDR3, in the form of F(ab) and $F(ab')_2$ fragments, have been shown bind MBL is not convincing to support the broad

recitation of the claims, as applicant is reminded that F(ab) and F(ab')$_2$ fragments also comprise CDR1 and CDR2 regions and comprise both the heavy chain variable region and the light chain variable region, meaning that the Ab fragments have CDR1, CDR2, and CDR3 contributions from both chains. Accordingly, the ground of rejection is deemed proper.

Information Disclosure Statement

4. Applicant's submission of Search Reports on the IDS filed March 25, 2003 is acknowledged, however these citations have been crossed out, as they are not appropriate for an IDS.

Allowable Subject Matter

5. Claims 30-32 are allowed.

Conclusion

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (703) 305-4441. The examiner can normally be reached on M-Th 6:30-4:00; Alternate Fridays 6:30-3:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 305-3014. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

F. Pierre VanderVegt, Ph.D.
Patent Examiner
June 23, 2003

PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
TECH CENTER 1600
6/26/03